The application has been amended as requested in the communication filed October 18, 2004. Accordingly, claims 2, 4, and 6 have been canceled, and claims 1, 3, 7, 8, 12, 38, 39, 48, and 49 have been amended.

Claims 1, 3, 7, 8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37-40, and 48-50 are under consideration in this Office action.

Claims 1, 3, 7, 8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37-40, and 48-50 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1652

Amendments to Claims

Claim 1 (Currently Amended). A method for the production of a carotenoid compound comprising:

(a) providing a transformed methylotrophic ~~C1 metabolizing~~ host cell comprising:

(i) ~~suitable levels of~~ isopentenyl pyrophosphate; and

(ii) at least one isolated nucleic acid molecule encoding an enzyme in the carotenoid biosynthetic pathway under the control of suitable regulatory sequences;

(b) contacting the host cell of step (a) under suitable growth conditions with an effective amount of a C1 carbon substrate, selected from the group consisting of methane and methanol whereby an carotenoid compound is produced.

Claim 2 (Canceled).

Claim 3 (Currently Amended). A method according to Claim 1 wherein the methylotrophic ~~C1 metabolizing~~ host cell is a ~~methylotroph~~ methanotroph selected from the group consisting of *Methylomonas, Methylobacter, Methhtylococcus, Methylosinus, Methylocyctis, Methylomicrobium, Methanomonas, and Methylophilus, ~~Methylobacillus, Methylobacterium, Hyphomicrobium, Xanthobacter, Bacillus, Paracoccus, Nocardia, Arthrobacter, Rhodopseudomonas, Pseudomonas, Candida, Hansenula, Pichia, Torulopsis,~~ and ~~Rhodotorula~~*

Claims 4-6 (Canceled).

Claim 7 (Currently Amended). A method according to Claim ~~6~~ 3 wherein the methanotrophic host is a high growth methanotrophic strain which comprises a functional Embden-Meyerhof carbon pathway, said pathway comprising a gene encoding a pyrophosphate dependent phosphofructokinase enzyme.

Claim 8 (Currently Amended). A method according to Claim 7 wherein the gene encoding a pyrophosphate dependent phosphofructokinase enzyme has the amino acid ~~seqeuene~~sequence as set forth in SEQ ID NO:2.

Claim 9 (Canceled).

Claim 10 (Original). A method according to Claim 7 wherein the high growth methanotrophic bacterial strain optionally contains a functional Entner-Douderoff carbon pathway.

Claim 11 (Canceled).

Claim 12 (Currently Amended). A method according to Claim 7 wherein the high growth methanotrophic ~~bacterial~~ strain is methylomonas 16a having the ATCC designation ATCC PTA 2402.

Claim 13 (Original). A method according to Claim 1 wherein the isolated nucleic acid molecule encodes a carotenoid biosynthetic enzyme selected from the group consisting of geranylgeranyl pyrophosphate (GGPP) synthase, phytoene synthase, phytoene desaturase, lycopene cyclase, β-carotene hydroxylase, zeaxanthin glucosyl transferase, β-carotene ketolase, β-carotene C-4 oxygenase, β-carotene desaturase, spheroidene monooxygenase, carotene hydratase, carotenoid 3,4-desaturase, 1-OH-carotenoid methylase, farnesyl diphosphate synthetase, and diapophytoene dehydrogenase.

Claim 14 (Canceled).

Claim 15 (Original). A method according to Claim 13 wherein the geranylgeranyl pyrophosphate (GGPP) synthase as the amino acid sequence as set forth in SEQ ID NO:.26.

Claim 16 (Canceled).

Claim 17 (Original). A method according to Claim 13 wherein the phytoene synthase as the amino acid sequence as set forth in SEQ ID NO:34.

Claim 18 (Canceled).

Claim 19 (Original). A method according to Claim 13 wherein the phytoene desaturase as the amino acid sequence as set forth in SEQ ID NO:32.

Claim 20 (Canceled).

Claim 21 (Original). A method according to Claim 13 wherein the lycopene cyclase as the amino acid sequence as set forth in SEQ ID NO:30.

Claim 22 (Canceled).

Claim 23 (Original). A method according to Claim 13 wherein β-carotene hydroxylase as the amino acid sequence as set forth in SEQ ID NO:36.

Claim 24 (Canceled).

Claim 25 (Original). A method according to Claim 13 wherein zeaxanthin glucosyl transferase as the amino acid sequence as set forth in SEQ ID NO:28.

Claim 26 (Canceled).

Claim 27 (Original). A method according to Claim 13 wherein the isolated nucleic acid molecule encoding a carotenoid biosynthetic enzyme encodes a β-carotene ketolase having the amino acid sequence as set for the in SEQ ID NO:38.

Claim 28-34 (Canceled).

Claim 35 (Original). A method according to Claim 13 wherein the isolated nucleic acid molecule encoding a carotenoid biosynthetic enzyme encodes a farnesyl diphosphate synthetase having the amino acid sequence as set forth in SEQ ID NO:20.

Claim 36 (Canceled).

Claim 37 (Original). A method according to Claim 13 wherein the isolated nucleic acid molecule encoding a carotenoid biosynthetic enzyme encodes a diapophytoene dehydrogenase enzyme having the amino acid sequence selected from the group consisting of SEQ ID NO:22 and SEQ ID NO:24.

Claim 38 (Currently Amended). A method according to Claim 3~~1~~ wherein said methanotroph~~ic bacteria~~ is *methylomonas* 16a ATCC PTA 2402.

Claim 39 (Currently Amended). A method according to Claim 1 wherein ~~the suitable levels of~~ isopentenyl pyrophosphate ~~are~~ is provided by the expression of heterologous upper pathway isoprenoid pathway genes.

Claim 40 (Original). A method according to Claim 39 wherein said upper pathway isoprenoid genes are selected from the group consisting of D-1-deoxyxylulose-5-phosphate synthase (*Dxs*), D-1-deoxyxylulose-5-phosphate reductoisomerase (*Dxr*), 2C-methyl-d-erythritol cytidylyltransferase (*IspD),* 4-diphosphocytidyl-2-C-methylerythritol kinase (*IspE),* 2C-methyl-d-erythritol 2,4-cyclodiphosphate synthase *(IspF),* CTP synthase (*PyrG*), lytB, and GcpE.

Claim 41-47 (Canceled).

Claim 48 (Previously Amended). A method according to Claim 1 wherein the carotenoid compound is selected from the group consisting of antheraxanthin, adonixanthin, astaxanthin, canthaxanthin, capsorubrin, β–cryptoxanthin alpha-carotene, beta-carotene, epsilon-carotene, echinenone, gamma-carotene, zeta-carotene, alpha-cryptoxanthin, diatoxanthin, 7,8-didehydroastaxanthin, fucoxanthin, fucoxanthinol, isorenieratene, lactucaxanthin, lutein, lycopene, neoxanthin, neurosporene, hydroxyneurosporene, peridinin, phytoene, rhodopin, rhodopin glucoside, siphonaxanthin, spheroidene, spheroidenone, spirilloxanthin, uriolide, uriolide acetate, violaxanthin, zeaxanthin-β-diglucoside, and zeaxanthin.

Claim 49 (Currently Amended). A method for the over-production of carotenoid production in a transformed methylotrophic ~~C1 metabolizing~~ host comprising:

(a) providing a transformed methylotrophic ~~C1 metabolizing~~ host cell comprising:

(i) ~~suitable levels of~~ isopentenyl pyrophosphate; and

(ii) at least one isolated nucleic acid molecule encoding an enzyme in the carotenoid biosynthetic pathway under the control of suitable regulatory sequences; and

(iii) either:

1) multiple copies of at least one gene encoding an enzyme selected from the group consisting of D-1-deoxyxylulose-5-phosphate synthase (*Dxs*), D-1-deoxyxylulose-5-phosphate reductoisomerase (*Dxr*), 2C-methyl-d-erythritol cytidylyltransferase (*IspD),* 4-diphosphocytidyl-2-C-methylerythritol kinase (*IspE),* 2C-methyl-d-erythritol 2,4-cyclodiphosphate synthase *(IspF),* CTP synthase (*PyrG*) lytB and gcpE; or

2) at least one gene encoding an enzyme selected from the group consisting of D-1-deoxyxylulose-5-phosphate synthase (*Dxs*), D-1-deoxyxylulose-5-phosphate reductoisomerase (*Dxr*), 2C-methyl-d-erythritol cytidylyltransferase (*IspD*), 4-diphosphocytidyl-2-C-methylerythritol kinase (*IspE*), 2C-methyl-d-erythritol 2,4-cyclodiphosphate synthase (*IspF*), CTP synthase (*PyrG*), lytB and gcpE operably linked to a strong promoter.

(b) contacting the host cell of step (a) under suitable growth conditions with an effective amount of a C1 carbon substrate, selected from the group consisting of methane and methanol whereby a carotenoid compound is over-produced.

Claim 50 (Original). A method according to Claim 49 wherein the at least one gene encoding an enzyme of either part (a)(iii)(1) or (a)(iii)(2) encodes an enzyme selected from the group consisting of SEQ ID NO:6, 8, 10, 12, 14, 16, and 18.

100% = SEQ ID NO: 9 of 10/700,003